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THE MECHANISM OF EVOLUTION

IN THE LIGHT OF HEREDITY AND DEVELOPMENT

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V. THE CELLULAR BASIS OF ONTOGENY AND PHYLOGENY

A. GERM CELLS AND SOMATIC CELLS

1. *Germ Cells the only Living Bond between Generations and Species*

IMAGINE the amazement and incredulity of the naturalists of a former generation, who thought of evolution only as the transformation of developed organisms under the influence of changing environment, if they could learn that to-day the greatest problems of ontogeny and phylogeny center in the structures and functions of the germ cells! And yet this is strictly and literally true. The germ cells form the only living bond not only between generations but also between species. The germ cells contain the physical basis not only of heredity but also of evolution. We know little about the changes taking place in germ cells which cause evolution, we are at present unable to initiate and control such changes, but at least we know where to look for them. The mechanism of evolution is at present largely unknown, but at least we know where that mechanism is located.

2. *Germ Cells and Somatic Cells are Fundamentally Alike*

When once the fact of the importance of the germ cells in ontogeny and phylogeny was appreciated there arose a belief that these cells must be essentially different from all other kinds of cells. Germ cells were contrasted with somatic cells and it was supposed that there must be a world-wide difference between cells which could give rise to new individuals or new species and those which constituted the various tissues of the body. And yet in many respects these cells are very similar. Both have a nucleus and a cell-body; in both the nucleus contains chromosomes that are usually of the same number, shape and relative size in all cells of a given species and while the cell-body of somatic cells undergoes marked differentiations in the various tissues these differentiations are probably no greater than the corresponding differentiations in the germ cells. Indeed the differentiations of a mature spermatozoon are probably as great as those of any muscle cell or nerve cell and the differentiations of the egg are as marked as those of any gland cell, while the differences between the male and female germ cells are quite as great as the differences between a muscle cell and a nerve cell. Furthermore there are many evidences that up to a certain stage of development cells may differentiate in one direction or another depending upon environmental conditions. Many cells which under certain conditions would have formed tissue cells may under other conditions form germ cells and *vice versa,* and this is especially true among lower organisms where cell differentiations appear more slowly and do not go so far as among higher forms. Such changes in the fate of a cell can not take place after differentiations have passed a certain stage; fully developed muscle cells or nerve cells can not become germ cells, nor can fully developed germ cells become tissue cells except by the process of embryonic development; but this means only that there is a critical stage in development beyond which differentiation is not a reversible process. All kinds of tissue cells as well as germ cells develop out of germ cells and it is evident that there is no *fundamental* distinction between the two.

3. *Nucleus (Germplasm) and Cytoplasm (Somatoplasm) are Fundamentally Different*

But while there is no fundamental difference between germ cells and somatic cells there is in every cell, excepting perhaps the very simplest organisms such as bacteria, a fundamental difference between nucleus and cytoplasm. Chemically and physically, morphologically and physiologically these two constituents of all cells are sharply distinguished. First of all there is a marked chemical difference between the two; the nucleus is acid in reaction, the cytoplasm alkaline; the nucleus contains a relatively large amount of phosphorus, the cytoplasm almost none at all; many compounds, especially nucleinic acid and nucleo-proteins are found exclusively in the nucleus. The nucleus is usually more dense and more highly refractive than the plasma.

But it is in morphological and physiological characteristics that the differences between nucleus and plasma reach a climax. The peculiarities of nuclear membrane and linin framework, of nuclear sap and chromatic granules, of chromosomes and nucleoli are too well known to need emphasis. And when to these morphological peculiarities of the nucleus are added its physiological characteristics,—its indispensability in constructive metabolism, regulation and regeneration, its control over cell-differentiation and development, its peculiarities of division, its unfailing continuity from cell to cell and from generation to generation,—it will be seen that this contrast between nucleus and plasma is fundamental. Although germ cells and somatic cells are not essentially unlike, nucleoplasm and cytoplasm are, and there is abundant evidence that germplasm is located in the nucleus, somatoplasm in the cell-body.

4. *Cell Division*

From every point of view our knowledge of organisms has been greatly advanced by the prolonged and extensive study which has been devoted to cell division. The older views as to the origin of cells by "free formation" or *de novo* have been referred to in a previous section (p. 489) and these false views have been responsible for many erroneous theories of heredity and evolution which persist in one form or another to this day. On the other hand the doctrine of Remak (1841) that every cell comes from a preexisting cell by a process of division has been found to be universally true and has greatly influenced almost all lines of biological research.

It was at first supposed that both the cell-body and the nucleus always divided by a process of simple constriction; afterwards it was discovered that the nucleus usually divides in a much more complicated manner and although it is still generally held that the cell-body divides by simple constriction there are evidences that this also is much more complicated than has commonly been supposed.

Neither the nucleus nor the cell-body is a simple, homogeneous structure which may divide equally by simple mass constriction. The nucleus is really a compound structure composed of a larger or smaller number of karyomeres or nuclear units, while the cell-body contains many different structures; a simple mass constriction of the entire cell could not possibly divide all of these equally. Accurate division of a complex cell requires a special mechanism and this is found in *mitosis* or *karyokinesis.*

(*a*) *Mitosis or Indirect Nuclear Division.*—During stages of division there appears in the nucleus a number of deeply staining threads or rods, the chromosomes, while other threads which do not stain readily form a spindle-shaped figure. In most animals and in many of the lower plants there is in the cytoplasm opposite each pole of the spindle a star-shaped figure, the *aster,* with a minute body, the *centrosome,* at its center. The nuclear membrane then dissolves and its contents are set free into the cell body; in place of the nucleus there is left a spindle with the chromosomes gathered around its equator and with the centrosomes and asters at its two poles. Then each chromosome splits lengthwise into two daughter chromosomes and these halves move in opposite directions along the spindle toward its poles, where they unite to form the two daughter nuclei.

This process is known as *mitosis* or indirect nuclear division and its chief significance is found in the fact that each chromosome is divided into daughter chromosomes each of which is identically like the other.

In the meantime complicated movements are taking place in the cell-body outside of the nucleus, which move the mitotic spindle into a definite position in the cell, sort and localize various constituents of the cytoplasm and finally lead to the division of the latter in a plane passing through the equator of the spindle, thus completing the division into two cells.

(*b*) *Persistent Identity of Chromosomes.*—Although the chromosomes constitute so striking a part of a dividing nucleus they usually disappear entirely after division and in their stead one finds only a single nuclear vesicle containing a clear, non-staining fluid or gel, the *achromatin,* imbedded in which are the granules or threads of *chromatin.* Usually no trace of chromosomes can be seen in such a "resting" nucleus.

However the fact that the same number of chromosomes is usually found in every dividing nucleus of any given species, that these chromosomes split lengthwise into daughter chromosomes which then unite to form the daughter nuclei, and that at the next division the same number of chromosomes, having the same shapes and relative sizes, come out of a nucleus as went into it at the preceding mitosis,—these facts early gave rise to the hypothesis that in some way or other the chromosomes preserve their individuality or identity throughout the "resting" stage between successive divisions.

This hypothesis of the "individuality of the chromosomes" has now been verified in a number of cases by actually tracing certain chromosomes into the daughter nucleus and through the "resting" stage until they emerge at the next division as typical chromosomes. It is found that each chromosome absorbs fluid from the cytoplasm and swells up to form a chromosomal vesicle (Fig. 11). These vesicles then unite to form the daughter nucleus and usually the partition walls between vesicles disappear leaving what appears to be a single nuclear vesicle, but in certain favorable objects it can be seen that each chromosomal vesicle persists through the whole of the resting stage and at the next mitosis the chromatin granules within each chromosomal vesicle are drawn together into a chromosome which is in all respects similiar to the one from which that vesicle arose. Probably every chromosome exists as a chromosomal vesicle during the resting stage and as a condensed chromosome during division and thus persists from cell to cell and from generation to generation. Possibly other parts of a cell may preserve indefinitely their individuality or identity, but in the case of the chromosomes this is no longer a mere hypothesis but an established fact.

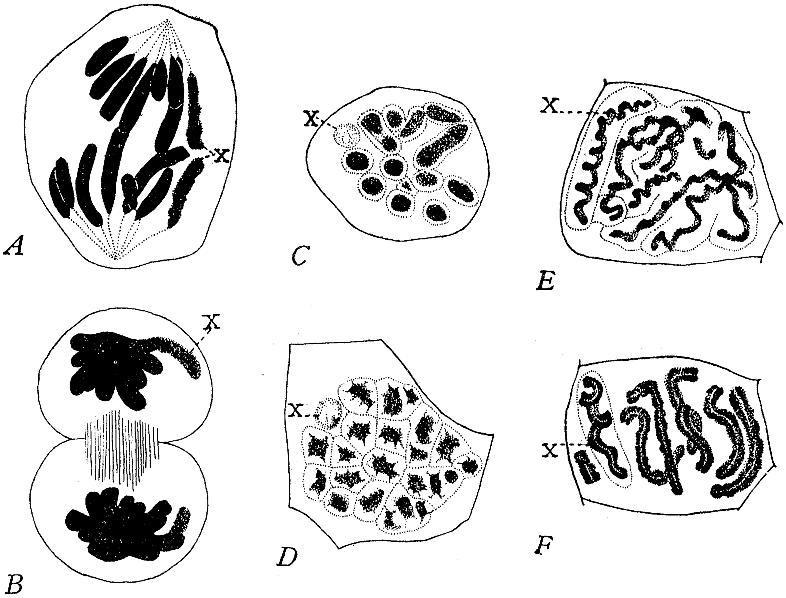

FIG. 11. SPERMATOGONIA OF *Phrynotettix*. *A* and *B*, Middle (metaphase) and late (anaphase) stages of mitosis showing separation of daughter chromosomes, among them the *X* (sex) chromosomes. *C* and *D*, Last stages (telophase) of mitosis passing into the resting nucleus; each chromosome is swelling up into a chromosomal vesicle. *E* and *F*, Early stages (prophase) of next division, showing the reappearence of a chromosome in each vesicle and in *F* the longitudinal splitting of every chromosome. (After Wenrich.)

A chromosome, like any living organism, undergoes many changes in its life cycle without losing its identity. The changes in form and staining reaction which it undergoes in passing from the resting to the dividing stage and *vice versa* indicate that persistent identity does not imply fixity of its entire organization. Nevertheless something, some part of that organization, must persist through all the changes of the division cycle, and it is evident that this is not the deeply-staining portion of the dividing chromosome for in the resting stage this chromatic material may lose its affinity for dyes and coincidently the nucleolus (karyosome) become chromatic, while these changes are reversed at the beginning of mitosis. Likewise in dessicated cells Hickernell found that the chromatic material moves to the periphery of the nucleus whereas in cells recovering from dessication it goes back into the nucleus. Consequently it seems probable that the persistent part of a chromosome is the achromatic framework or linin in which chromatin is present at certain phases of the cell cycle and absent at others, just as the persistent part of a red corpuscle is the cytoplasmic framework which may or may not contain hæmoglobin.

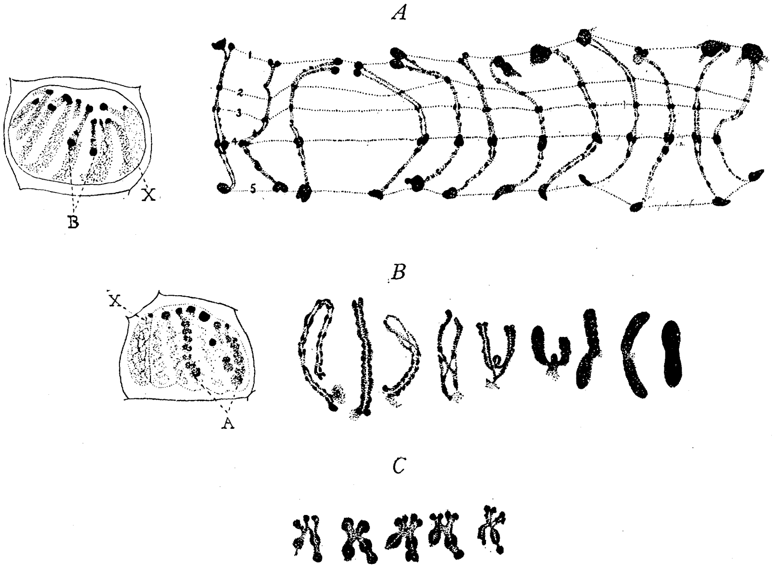

FIG. 12. SYNAPSIS (CONJUGATION) OF CHROMOSOMES IN *Phrynotettix*. *A*, Resting nucleus at left shows indistinct chromosomes, among them chromosome *X* and the pair *B*. At the right are 12 pairs of *B* chromosomes, each from a different animal, showing side by side conjugation of chromosomes of a pair and homologous chromomeres (1, 2, 3, 4) in each pair. *B*, Similar stages in chromosome pair *A*. Some of the chromosome pairs at the right show a secondary longitudinal split and a "crossing-over" of the halves. *C*, Tetrads (bivalent chromosomes) of chromosome pair *B*, formed by shortening and thickening of the chromosome pairs and by the appearance of the secondary split. (After Wenrich.)

There is evidence that the chromosomes themselves are compound structures and that just as nuclei are composed of chromosomes or their vesicles, so the latter are composed of smaller units, the chromatin granules or chromomeres. In the formation of chromosomes, the chromomeres appear like beads on a string and in the splitting of chromosomes each chromomere divides into equal halves, and just as the chromosomes are specific bodies each of which preserves its identity, so each chromomere is probably a specific and persistent body. Wenrich has shown that in certain chromosomes of a grasshopper there are specific chromomeres occupying particular positions and that some of these chromomeres preserve their identity throughout the resting stages and are therefore persistent structures (Fig. 12). In all probability further work will demonstrate that every chromomere in a chromosome is a specific and persistent body. Indeed it is probable that chromomeres are much more constant than chromosomes. McClung and his pupils have shown that the number of chromosomes in a given species or in related species may not always be constant, owing to the fact that certain chromosomes may fragment while in other cases separate ones may unite. But whatever the number of chromosomes may be there is apparently a constant number of chromomeres in every species, perhaps even in all closely allied species, and variations in the number of chromosomes are due to the grouping of the chromomeres into a larger or smaller number of chromosomes.

5. *Panmerism*

It is one of the characteristics of organisms and parts of organisms that they are capable of assimilation, growth and division. This is true not only of the larger units of organization but probably also of every unit down to the ultra-microscopic parts of cells and protoplasm. Indeed the larger and more complex units may lose this property while it is still retained by the smaller units. Entire organisms and organs may lose the power of continued growth and division while it is still retained by cells or parts of cells. By this process of growth and division every cell comes from a preceding cell, every nucleus from a nucleus, every chromosome from a chromosome, every chromomere from a chromomere, every gene from a gene, —and in general every vital unit from a preceding unit of the same kind. So far as is known the simpler units always divide equally both in size and quality; this is true of the units composing the nucleus such as chromosomes, chromomeres, genes and probably also of the individual units of the cytoplasm.

But entire cells or groups of cells may divide equally or unequally and the differentiations of development are due mainly to this fact. Such differential divisions of cells are due in the main to different combinations and localizations of units which divide equally and non-differentially, and *in general all forms of differentiation, variation, and evolution are due to different combinations of vital units, whether they be organs, tissues, cells, plastids, chromosomes, chromomeres, genes or subgenes;* just as all forms of chemical compounds are due to different combinations of some 80 chemical elements, and all words, sentences, languages and literatures are the result of different combinations of a small number of letters. However the smaller units of living organization grow and divide equally and not differentially and this property perpetuates the identity of particular kinds of units.

But it is not necessary to assume that everything capable of increasing its own substance is alive. Certainly many substances which are not protoplasm have this power. Ferments which are capable of self-propagation, or substances which produce ferments which in turn are capable of producing those substances, are known. Such reactions are called auto-catalytic and it is probable that many phenomena of reproduction, especially among the smaller units of organisms, are autocatalytic reactions. We do not know whether in such reactions colloidal particles, or molecular aggregates, grow and divide, but this is just what takes place in the parts of cells which are visible with the microscope. These parts of cells are not alive in the sense or to the same extent that the entire cell is; they are incapable of continued independent existence, and it is probably as erroneous to hold that every minute unit of organization is composed of living protoplasm as it would be to regard every brick in a building as a minute house.

B. MECHANISM OF HEREDITY

The mechanism of heredity is to be found in the structure and functions of the germ cells, for everything that is transmitted from one generation to the next must be through the germ cells. The method of studying this mechanism must be by the correlation of particular features of the germ cells with particular phenomena of heredity, in short by the cooperation of cytology and genetics.

1. *Chromosomes and Inheritance Units*

It was pointed out on a previous page that there are many reasons for supposing that the germplasm is located in the nucleus, the somatoplasm in the cell body. Furthermore the chromosomes more nearly fulfill the requirements of an inheritance material than any other constituents of the nucleus. The evidence that the Mendelian factors or genes are located in the chromosomes may be summarized as follows:

(*a*) *General Equivalence of Germplasm and of Chromosomes in Egg and Sperm.*—A study of heredity shows that on the whole offspring inherit as much from one parent as from the other and therefore as many genes must be derived from the sperm as from the egg. But the only substances which are known to come in approximately equal quantities from the two sex cells are the chromosomes. The egg at the time of fertilization contains a relatively large quantity of cytoplasm, yolk and other substances in the cell-body. The spermatozoon, on the other hand, is one of the smallest of all cells and usually its head only enters the egg, leaving the tail and most of the cytoplasm outside. The head of the spermatozoon consists almost entirely of a condensed nucleus in which is the characteristic number of chromosomes. In the egg nucleus also this characteristic number of chromosomes is present. The egg and sperm nuclei come together within the egg and their chromosomes mingle but do not fuse together nor lose their identity. The chromosomes which come from the egg and those from the sperm are not only equal in number and size but are also alike in shape so that in every fertilized egg there are two sets of similar chromosomes, one set from the egg and the other from the sperm. The chromosomes are the only portions of the male and female germ cells which are approximately equal in volume and it is therefore probable that they are the seat of the inheritance material.

(*b*) *Equal Distribution to all Cells.*—Since inherited characters of one or the other parent may appear in every part of the bodies of offspring, it must be that inheritance units from the two parents are distributed equally to every cell. So far as known the only portions of the egg and sperm which are distributed equally to every cell of the developing organism are the chromosomes. At the first division of the fertilized egg and at every subsequent division each chromosome divides equally and its halves go into the two daughter cells. Therefore every cleavage cell, and ultimately every cell of the adult body comes to contain one full set of chromosomes from the egg and another set from the sperm. Since the chromosomes are the only portions of the egg and sperm which are known to be distributed equally to every cell, it is probable that they contain the inheritance factors.

(*c*) *Conjugation and Reduction of Maternal and Paternal Chromosomes.*—In the last stages of the formation of the germ cells the two sets of parental chromosomes temporarily unite, and in general long chromosomes pair with long ones, short ones with short ones and those of peculiar shape with others of similar shape; in short the members of each pair are homologous

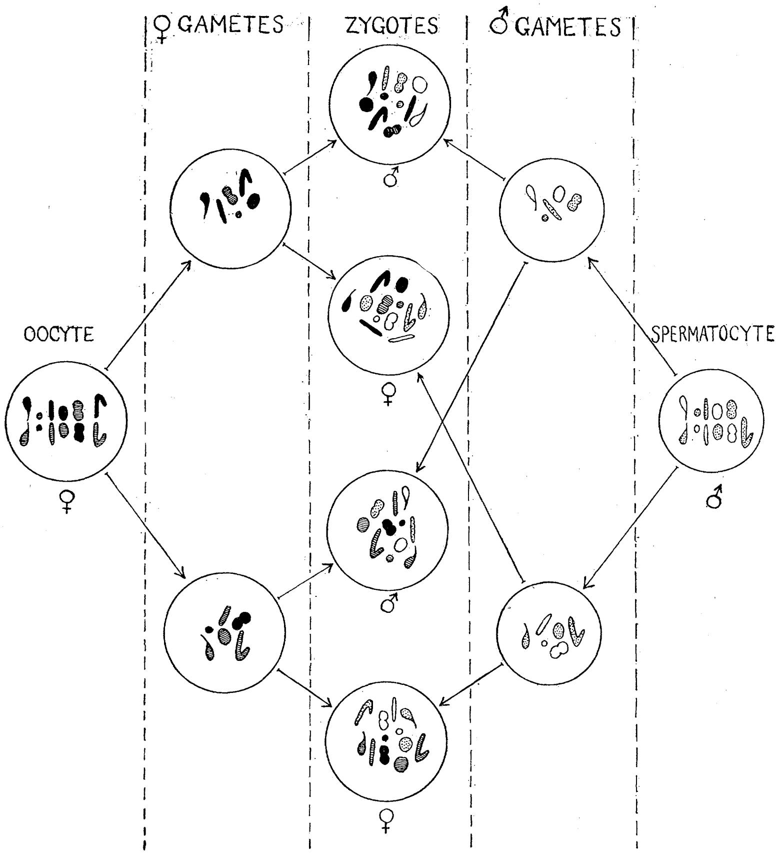

FIG. 13. DIAGRAM SHOWING SOME OF THE POSSIBLE DISTRIBUTIONS OF CHROMOSOMES OF GRANDPARENTS TO GRANDCHILDREN. Chromosomes of paternal grandfather unshaded, of paternal grandmother stippled, of maternal grandfather with cross lines, of maternal grandmother black. The sex chromosomes are *J*-shaped, a pair being present in the female and a single one in the male. In the oocyte and spermatocyte synaptic pairs of homologous chromosomes are shown separating so that the gametes contain only one of each pair. By the union of gametes to form zygotes the double number is restored.

chromosomes. This process is known as *synapsis* or the conjugation of the chromosomes, the pairs are called synaptic pairs or bivalent chromosomes; and in some cases it can be demonstrated that one member of each pair comes from the father, the other from the mother (Figs. 12, 13, 15, 16).

In all ordinary divisions every chromosome splits into two and the halves go into the daughter cells, but in one or the other of the last two divisions leading to the formation of the germ cells, the synaptic pairs separate, whole chromosomes going into the daughter cells. By the separation of whole chromosomes in this division the germ cells come to contain only one half as many chromosomes as the other cells of the body. The full number of chromosomes is the diploid number ($2n$), the reduced number the haploid ($1n$) and the division by which this reduction is effected is known as the "reduction division." On the other hand ordinary divisions, in which each chromosome splits and the daughter cells contain as many chromosomes as the mother cell, are known as "equation divisions."

Since one chromosome of each synaptic pair is from the father and the other from the mother and since these chromosomes separate freely in the reduction division, that is each member is free to move to either pole of the mitotic spindle, it follows that each germ cell or gamete contains one full set of chromosomes, some of which are from the father and others from the mother, but only one chromosome of each pair is found in any gamete (Fig. 13).

The correlation between these cytological facts and the phenomena of heredity are very striking. All hybrids carry two sets of factors, derived from the two parents, but in the formation of the gametes these factors separate so that every germ cell is pure with respect to any character. In this respect the factors, which are invisible, behave exactly as do the chromosomes which are easily seen. Indeed it would be impossible to invent a more perfect mechanism for the segregation of Mendelian factors than is found in the union of maternal and paternal chromosomes into synaptic pairs and their subsequent separation in the reduction division. This complete parallelism between the behavior of the chromosomes and of the inheritance factors is convincing evidence that the factors are located in the chromosomes (Figs. 14, 15).

(*d*) *Doubling of Chromosomes and of Factors in Fertilization.*—Finally in the union of male and female gametes, each having the reduced or haploid number of chromosomes, the somatic or diploid number is restored. The chance combination of chromosomes in fertilization is identically like the chance combinations of inheritance factors, and both yield the same Mendelian ratios. Mendelian segregation and recombination of factors is exactly parallel to the reduction of chromosomes in gametogenesis and their union in fertilization. In every respect chromosomes may stand as the visible symbols of factors (Figs. 14, 15). It is highly probable therefore that the factors are located in the chromosomes.

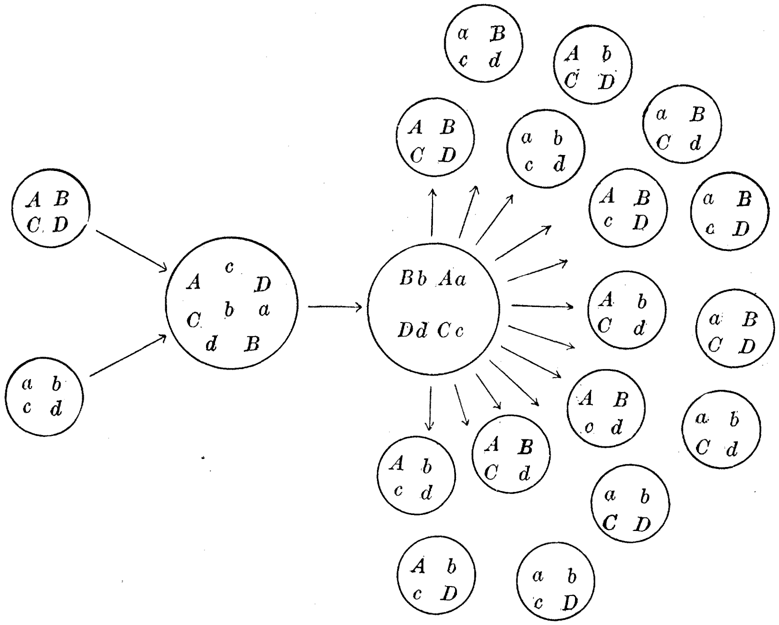

FIG. 14. DIAGRAM SHOWING UNION IN FERTILIZATION, CONJUGATION IN SYNAPSIS AND SEGREGATION IN FORMATION OF GAMETES of Factors *A, B, C, D* of the egg and *a, b, c, d,* of the sperm. (After Wilson.)

(*e*) *Sex-Determination and "Sex-Chromosomes."*—Still further evidence that the chromosomes are the seat of inheritance factors is found in the relation of some of these bodies to sex-determination.

The cause of sex has been a subject of speculation and theorizing for hundreds if not thousands of years, but within the last fifteen years it has been discovered that at least the initial cause of the differentiation of the two sexes is inherited, although there may be many other causes which are environmental. In this respect sex does not differ from any other inherited character; many causes both hereditary and environmental are involved in the *development* of any inherited character; all that is implied in saying that any character is *inherited* is that its initial differential is transmitted through the germ cells.

In this sense it is known that in many animals and plants sex is inherited as a Mendelian character, one sex being homozygous and the other heterozygous for this character and that consequently the heterozygous sex forms two sorts of germ cells, the homozygous but one and the chance combination of these germ cells yields equal numbers of homozygotes and heterozygotes, which fact explains the numerical equality of the two sexes.

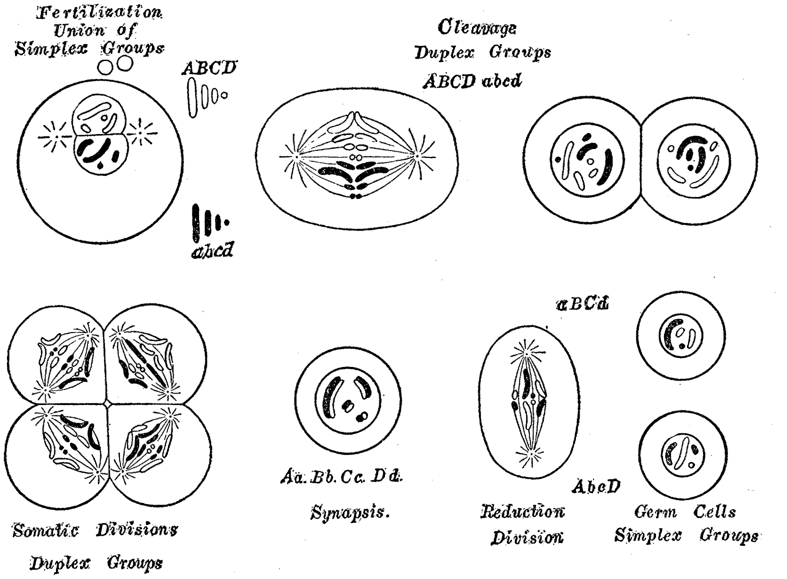

FIG. 15. DIAGRAM OF UNION OF CHROMOSOMES OF EGG AND SPERM IN FERTILIZATION, THEIR CONJUGATION IN SYNAPSIS AND SEGREGATION IN FORMATION OF GERM CELLS, corresponding to the factors shown in Fig. 14. (After Wilson.)

In all such instances we have a plain Mendelian case of the crossing of a heterozygous with a homozygous form in which one half of the offspring are homozygous and the other half heterozygous, as shown in the following scheme:

Female (homozygous) produces Eggs of one type....... = ♀ ↖ — ↗ ♀
↑ X ↑
Male (heterozygous) produces Sperms of two types...... = ♀ ╱ — ╲ ♂
All possible crosses result in.......................... =2♀♀ : 2(♀)♂

or the ratio of males to females is 1 : 1.

In the spermatogenesis of certain insects it had been observed that there was an odd number of chromosomes and in synapsis when homologous maternal and paternal chromosomes unite in pairs one of these chromosomes was left without a mate; it was therefore called the "odd" or "accessory" chromosome. In the reduction division when the two chromosomes of a pair separate the odd chromosome went entire to one pole of the mitotic figure and there was no corresponding chromosome at the other pole; consequently, one of the two gametes formed by this division had one chromosome more than the other and two types of spermatozoa were formed in equal numbers,—one type with and one without the "odd" chromosome (Fig. 16).

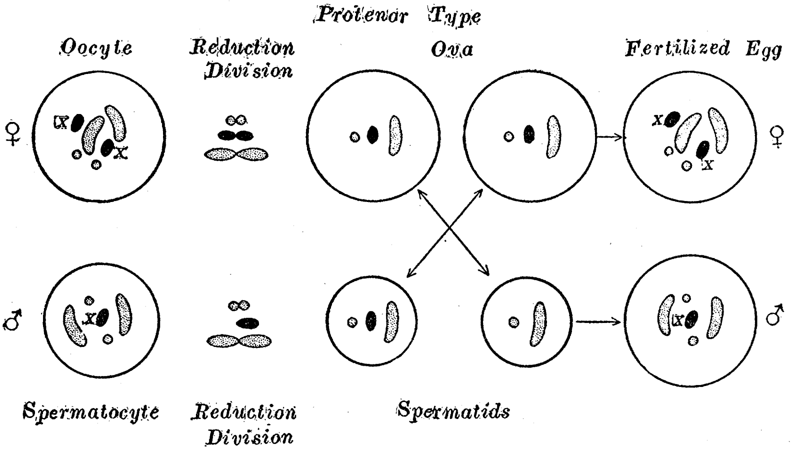

FIG. 16. DIAGRAM OF CHROMOSOMAL DETERMINATION OF SEX IN *Protenor* (*XO* TYPE). The oocyte contains 6 chromosomes, 2 of them being sex chromosomes (*X*), the spermatocyte contains 5, there being only 1 *X*; after reduction each egg contains 1 *X* and 2 ordinary chromosomes; half of the spermatozoa contain 1 *X* and the other half lack it; if an egg is fertilized by a sperm with an *X* a female results, if by one without the *X* a male is produced. (After Wilson.)

Since the 1:1 ratio of these two types of spermatozoa corresponds to the usual sex ratio, McClung suggested that this "odd" chromosome was a sex determinant. Wilson and Stevens then found that all eggs contain this "odd" chromosome, which was therefore called the "sex" chromosome, or the "*X*" chromosome, and that any egg fertilized by a sperm containing this chromosome produced a female, whereas if fertilized by a sperm without it a male was produced, as is shown in the following diagram:

Chromosomal Constitution of Male (♂) Zygote *XO*, of Gametes.
of Female (♀) " *XX*, " " .

$$\begin{tikzcd} X \arrow[d] \arrow[dr] & O \arrow[d] \arrow[dl] \\ X & X \end{tikzcd}$$

All posible combinations of these Gametes (indicated by arrows) 2XX(♀) : 2XO(♂)

Later Wilson and Stevens discovered that in the males of certain other insects the "odd" chromosome had a mate which was small or rudimentary and which they called the "*Y*" chromosome. Consequently the sex chromosomes of the male were in these cases *X* and *Y*, while those of the female were *X* and *X* and the chance combinations of the gametes formed by these animals yielded equal numbers of the combination *XY* (♂) and *XX* (♀) (Fig. 17).

At present it is known in more than one hundred species of animals and plants that with respect to the sex chromosomes two types of spermatozoa occur and but one type of ova, that eggs fertilized by one type of sperm produce males and by the other type females. In a few cases among Lepidoptera and birds there is evidence that the female is heterozygous for sex, the male homozygous, and that correspondingly two types of ova are produced and but one type of spermatozoa; but this does not affect the general principle that sex is determined by the chance union of gametes bearing particular sex chromosomes.

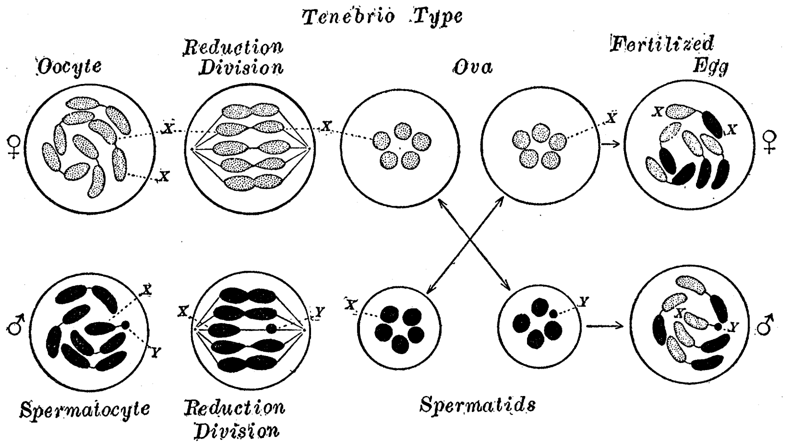

FIG. 17. DIAGRAM OF CHROMOSOMAL DETERMINATION OF SEX IN *Tenebrio* (*XY* TYPE), showing 5 synaptic pairs of chromosomes (there are actually 10 pairs). In the oocyte the sex chromosomes (*XX*) are equal in size and after reduction each ovum contains 1 *X*; in the spermatocyte these chromosomes are unequal (*XY*) and after reduction half of the spermatozoa contain a large *X* and half a small *Y*; sex is determined by the chance union of one or the other of these types of spermatozoa with the single type of ova.

This correlation between the presence or absence of a whole chromosome and of a developed character such as sex, is the only case of the kind that is known and more than anything else it has served to prove that the chromosomes contain the Mendelian factors. The absence of a whole chromosome is plainly visible under the microscope, whereas the absence of a single factor or gene from a chromosome would never have been seen. These fortunate cases in which the male lacks a whole chromosome give ocular proof of the chromosomal theory of heredity.

Environmental Influences.—It should be said that a number of apparent exceptions to the chromosomal determination of sex are known. In some of these cases environmental conditions change the usual 1:1 sex ratio or lead to the development of "intersexes" which are more or less intermediate between males and females. Departures from the normal sex ratio are sometimes due to the early death of one type of gametes or zygotes; "intersexes" may be caused by a balancing of male-producing and female-producing factors in the zygote, or of conflicting genetic and environmental factors in development. These cases illustrate the necessity of distinguishing between the hereditary determination of sex and its ontogenetic development.

Probably in every case these apparent exceptions to the chromosomal determination of sex may be explained in conformity with that theory; in any event this theory is now so well established in so many different cases that it may be accepted as the usual if not the only method of sex determination. But this means only that the initial factors for sex *determination* are carried in a particular chromosome. Doubtless there are many other factors in the *development* of sex, some of which are germinal and others environmental.

The male or female condition may be regarded, therefore, as the result of the dominance of male-determining or female-determining factors, and the condition of "intersexes" as the result of the partial dominance of one or both of these factors. This applies of course to the primary sex characters, such as ovaries and testes, and also to secondary characters which are associated with one or the other sex, such as peculiarities of size, color, hair or feathers, mammary glands, voice, instincts and habits, etc. The full development of these secondary sex characters is usually limited to one sex or the other; they are known as *sex-limited* characters and their development is dependent upon the dominance of the male-determining or the female-determining factors, whether those factors be hereditary or environmental.

Sex-linked Characters.—Another class of characters which Morgan has called *sex-linked* are inherited in the same way that sex itself is and for the reason, as he has proved, that their genes are located in the sex-determining chromosome. These characters may have nothing to do with sex itself but their genes are linked with those of sex. Morgan has found a large number of such sex-linked characters in the pomice fly, *Drosophila melanogaster,* among them eye-color, body-color, wing characters, etc. Other well-known cases are Daltonism or color blindness and hemophilia or slow clotting of blood in man.

Such sex-linked characters are like recessive ones in that they do not develop when balanced by a normal allelomorph. Consequently they do not develop in females unless they are inherited from both parents, their genes being present in both *X* chromosomes, whereas in males they are always inherited from the mother only since the single *X* chromosome of the male always comes from the mother. All the sons of a color-blind father and normal mother are normal since the single *X* chromosome which they have comes from the mother and carries the gene for normal vision. All the daughters of such a cross appear normal, although carrying the paternal gene for color-blindness, since they also have from their mother the gene for normal vision. Half of the germ cells of these daughters carry the gene for color-blindness, half for normal vision and if one of the former kind is fertilized by a male-producing

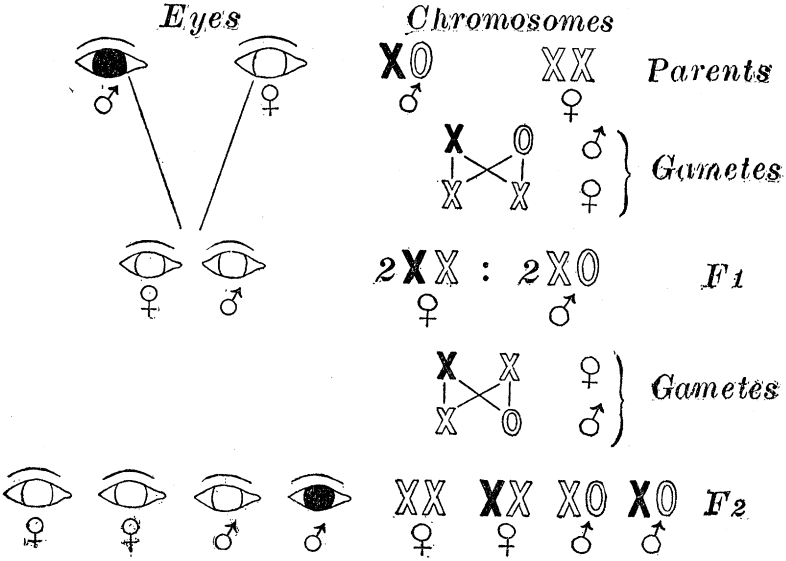

FIG. 18. DIAGRAM OF SEX-LINKED INHERITANCE OF COLOR-BLINDNESS (DALTONISM). A color-blind male (here black) transmits his defect to one half of his grandsons only. The corresponding distribution of the sex chromosome containing the gene for this defect is shown on the right. (After Morgan.)

sperm it gives rise to a color-blind male since in this case the gene for color-blindness is not balanced by a normal allelomorph; consequently half of the sons of the F_2 generation will be color blind (Fig. 18).

(*f*) *Abnormal Distribution of Chromosomes and Factors.* —Experimental evidence that the chromosomes are the seat of inheritance factors is found in the correlation between the abnormal distribution of chromosomes and the development of abnormal characters in the embryo or adult. An abnormal distribution of chromosomes to the cleavage cells may be caused in a variety of ways but one of the least injurious methods of accomplishing this is by causing two spermatozoa instead of one to enter an egg. In such doubly fertilized eggs Boveri discovered that different cleavage cells receive a different number of chromosomes and in general those cells which receive the largest number develop most typically, while those which receive a small number develop atypically. By a skillful analysis Boveri proved that normal development depends not so much upon the absolute number of chromosomes in a given cell as upon a complete set of all the different kinds of chromosomes, and when a complete set was not present certain characters were lacking in development. By this means he showed that different chromosomes of a set differ in hereditary value, as, for example, the fingers of a hand differ from one another, and that two chromosomes of one kind could not make up for the lack of one of another kind, any more than two thumbs could make up for the loss of a little finger.

A still more detailed correlation between the presence or absence of a particular chromosome and the presence or absence of particular characters in the developed organism has been described by Bridges (1916). In his study of the pomice fly, *Drosophila melanogaster,* he found that the occasional appearance (1 in 1700) of a matroclinous daughter or patroclinous son was due to the fact that the *XX* pair of chromosomes fail to separate in the reduction division of the egg so that both *XX*'s are included in the egg (Fig. 20, *C*) or both are extruded in the polar body, or the *XY* pair fail to separate in the reduction division of the sperm so that one sperm may have both and another lack both of these chromosomes. This phenomenon he calls "non-disjunction" and it results in the production of matroclinous daughters or patroclinous sons, and in many other irregularities of inheritance which follow precisely the abnormal distribution of these chromosomes. A patroclinous son is the result of the fertilization of an *O* egg by an *X* sperm; such an *XO* son is sterile whereas the normal *XY* son is not, thus showing that the chromosome *Y* has some function though apparently it does not contain any of the genes; fertilization of an *O* egg by a *Y* sperm produces a combination (*YO*) which is non-viable. Fertilization of an *XX* egg by a *Y* sperm produces a matroclinous daughter (*XXY*), whereas fertilization of an *XX* egg by an *X* sperm produces a combination (*XXX*) which is non-viable. These relations are shown schematically in the accompanying diagrams (Fig. 19).

Finally the most notable correlation between abnormal distribution of chromosomes and the development of abnormal characters has been found by Morgan in gynandromorphs or sex-mosaics of *Drosophila* in which one portion of the body has the characters of the male and another those of the female. Such sex-mosaics are evidently due to the fact that in the ordinary somatic cell-divisions the pair of *XX* chromosomes in the female or of *XY* chromosomes in the male do not go into every daughter cell but are so distributed that two *X*s (female constitution) occur in some cells and one *X* (male constitution) in other cells.

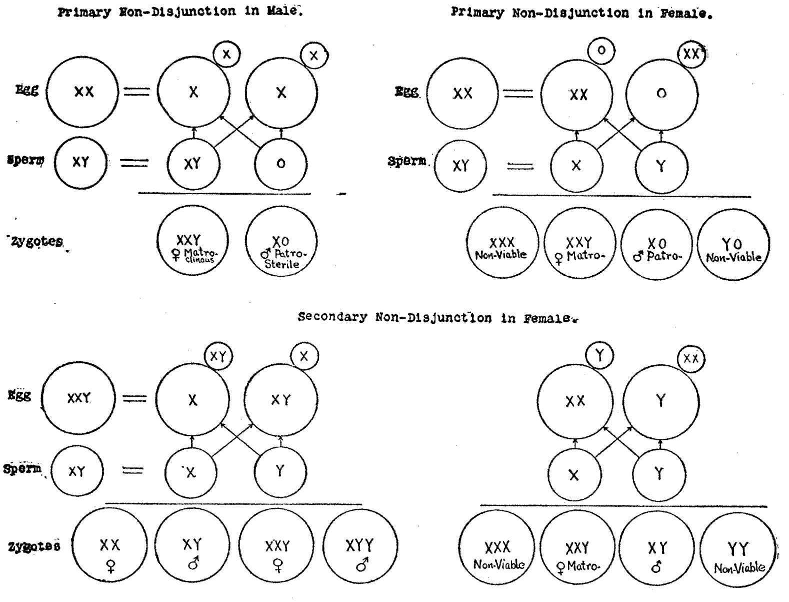

FIG. 19. DIAGRAM OF NON-DISJUNCTION OF SEX CHROMOSOMES (BRIDGES) IN THE MATURATION OF THE EGG AND SPERM AND THE RESULTING TYPES OF ZYGOTES.

All of these cases of abnormal distribution of chromosomes coincide exactly with the subsequent abnormal distribution of characters in the developed animal and they prove that the inherited factors for these characters are located in the chromosomes.

(*g*) *Linkage of Characters and Chromosomal Localization.*—Finally the study of characters which are linked together in heredity, joined with the study of the chromosomes and their distribution in the maturation and fertilization of the germ cells, has not only confirmed the chromosomal theory of heredity but has also shown that certain chromosomes carry the genes for certain characters and has even indicated the relative positions of different genes in the chromosomes.

In higher animals and plants the number of chromosomes is small as compared with the number of their Mendelian factors, and therefore if these factors are located in the chromosomes each must contain several of them. Since chromosomes generally preserve their identity or individuality the factors which they contain should be linked together and developed characters should be inherited in groups corresponding in number to the different chromosomes.

It has been known for a long time that certain characters are correlated so that they usually go together although they may have no evident dependence upon one another. Thus Darwin mentions the fact that male albino cats with blue eyes are usually deaf and have defective teeth. Many other cases of the association of peculiar characters were reported by earlier and later observers but the causes of such correlations were wholly unknown.

Since 1910 Morgan and his associates have discovered more than one hundred new characters, or mutations, in the pomice fly, *Drosophila melanogaster,* which are linked together into four groups, corresponding to the four pairs of chromosomes in this species. Up to 1916 they had located in the first group 47 different characters, in the second 27, in the third 22 and in the fourth 2.

Corresponding with the number and size of these groups there are four pairs of chromosomes in *Drosophila,* three of which are large and one is very small (Fig. 20). The sex chromosomes (*XY* in the male, *XX* in the female) constitute one of the large pairs and the genes of the characters which are sex-linked are located in these chromosomes; the genes of the second and third groups of characters are presumably in the other large chromosomes, while the fourth group of only two characters probably have their genes in the very small chromosomes. If this interpretation is correct, linkage is due to the grouping together of certain genes in certain chromosomes, there are as many groups of characters as there are pairs of chromosomes and as long as the chromosomes preserve their individuality the linkage of genes in the chromosomes and of characters in the developed organism will persist.

"Cross-Overs."—But linkage of inherited characters is not quite so simple as this statement would indicate for an extensive study of this phenomenon in *Drosophila* has shown that while characters are usually inherited in the same groups this is not always true. For example, Morgan has found that when a female fly with white eyes and yellow wings is crossed to a male with red eyes and gray wings all the sons are yellow and have white eyes while all the daughters are gray and have red eyes, but when these latter are crossed 99 per cent. of the offspring show the same linkage of the colors yellow-white, gray-red, but in 1 per cent. the linkage is yellow-red, gray-white.

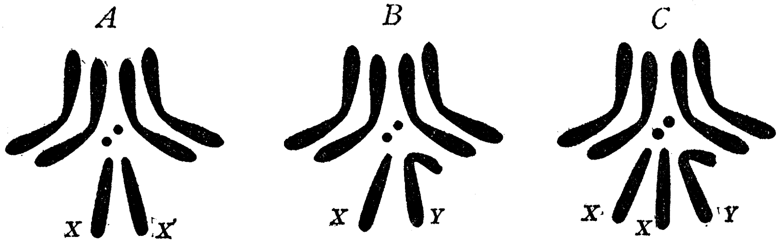

FIG. 20. CHROMOSOMES (DIPLOID NUMBER) OF *Drosophila melanogaster*. *A*, Female with 2 *X* chromosomes; *B*, Male with 1 *X* and 1 *Y*; *C*, Matroclinous female resulting from non-disjunction of the 2 *X* chromosomes of the egg. (After Morgan.)

This interchange of characters in the two groups, or "cross-over" as Morgan calls it, may be explained by assuming that there has been an interchange of genes between the two sex chromosomes of the female; "cross-overs" do not occur in the male of *Drosophila*. Janssens has found that when the paired chromosomes lie side by side in synapsis they sometimes twist around each other and in their subsequent separation each chromosome sometimes breaks at the point where the two cross and a portion of one chromosome is thereafter joined to the other one. In this "chiasmatype" of Janssens we have a relatively simple explanation of the interchange or "cross-over" of genes and consequently of the breaking up of old groups of characters and the establishment of new ones. Similar regrouping of characters takes place in each of the other three groups of *Drosophila* and can be explained in the same way (Fig. 21). If chromosomes of a pair are twisted round each other at more than one place and are then broken at these points we get double or multiple crossing-over and a corresponding re-grouping of genes and of characters. Unless a pair of chromosomes are very tightly twisted two cross-overs will not occur near together and in general the farther apart points are in a chromosome the more likely is a cross-over to occur.

All genes which are linked to each other lie in the same chromosome and Bridges (1914) has shown that the farther apart in a chromosome any two genes lie the greater is the amount of crossing-over between them. Morgan takes 1 per cent. of crossing-over as the "cross-over value" and in general this may be used as the unit of distance between genes in the same chromosome. If cross-overs between two genes take place only in one case out of a hundred (1 per cent.) the genes are supposed to be separated by only one (1) unit of distance; if in thirty cases out of a hundred (30 per cent.) they are separated by thirty (30) units, etc. And when the relative num-

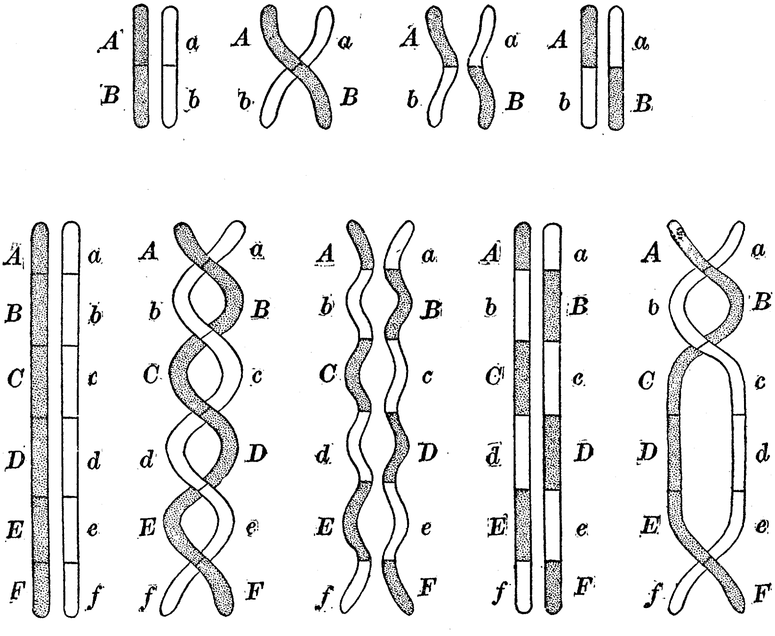

FIG. 21. DIAGRAM OF THE PROBABLE MECHANISM OF "CROSSING-OVER." Pairs of homologous chromosomes, one from the father the other from the mother, are shown in synapsis; on the left they lie parallel to each other and when they separate they remain as they were before union; in the second column they are shown crossing each other one or more times; in the remaining figures are shown the results of the chromosomes breaking at the points of crossing, thus interchanging sections of the two chromosomes. Letters indicate *loci* of homologous genes in the two chromosomes of a pair. (After Wilson.)

bers of all cross-overs are considered it is possible to construct a "map" of the chromosomes, as Morgan has done, showing the relative positions and distances apart of all the genes concerned.

Such a map represents only an approximation to the truth since certain conditions may change the percentage of cross-overs; thus Sturtevant has found that "factors for crossing-over" may be present in certain cases which modify the expected percentages, and Plough has shown that crossing-over may be increased by high temperatures, and that it takes place only in the *early oocyte* stage when the chromosomes are fine threads. Nevertheless these modifications of the percentages of cross-overs do not appear to invalidate the calculations as to the relative positions of genes in a chromosome.

Castle (1919, 1920) maintains that Morgan's evidence does not support the hypothesis of the linear arrangement of genes in a chromosome and he attempts to show that an arrangement of genes in three dimensions of space around the chromosomes is a more likely hypothesis. Without entering into the details of his argument it may be said that the longitudinal splitting of chromosomes, the equal division of genes, and the union of chromosome pairs in synapsis during the slender thread stage seem to admit of no other explanation than a linear arrangement of genes in the chromosome.

This work of Morgan and his associates on the localization of genes is in all respects the most remarkable work which has ever been done in this field; for the first time it gives us a detailed picture of what Weismann called the "architecture of the germplasm"—for the first time it assigns to different genes "a local habitation and a name."

(*To be continued*)